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Proposed Registration Decision PRD2017-06

1-Methylcyclopropene

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Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6607D
Ottawa, Ontario K1A 0K9

Internet: pmra.publications@hc-sc.gc.ca
healthcanada.gc.ca/pmra
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
pmra.infoserv@hc-sc.gc.ca

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Overview

Proposed Registration Decision for 1-Methylcyclopropene

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of 1-Methylcyclopropene (1-MCP) Technical and Harvista 1.3 SC to apple trees/orchards to slow ripening and delay harvest.

1-Methylcyclopropene is currently registered for postharvest use on stored food and feed. The detailed review of 1-Methylcyclopropene can be found in REG2004-07, *1-Methylcyclopropene*, PRD2007-11, *1-Methylcyclopropene* and RD2008-03, *1-Methylcyclopropene*.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of 1-Methylcyclopropene (1-MCP) Technical and Harvista 1.3 SC.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment. These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "... the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

Before making a final registration decision on 1-Methylcyclopropene, the PMRA will consider any comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on 1-Methylcyclopropene, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

What Is 1-Methylcyclopropene?

1-Methylcyclopropene is a plant growth regulator that inhibits ethylene, a plant hormone that promotes fruit ripening and senescence. 1-Methylcyclopropene applied to apples in the orchard delays the harvest by slowing fruit maturation. This delay results in fruit that are more likely to be picked at the optimum stage of maturity thereby maximizing and preserving fruit quality.

Health Considerations

1-Methylcyclopropene is unlikely to affect human health when it is used according to label directions.

Potential exposure to 1-Methylcyclopropene may occur when loading, and/or applying the product, as well as during clean-up and repair activities. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100 times higher (and often much higher) than levels to which humans are normally exposed when pesticide products are used according to label directions.

In laboratory animals the technical grade active ingredient, 1-Methylcyclopropene (1-MCP) Technical, containing 1-methylcyclopropene, is of low acute toxicity. Skin and eye irritation, and dermal sensitization were not determined because the technical grade active ingredient is a gas at room temperature.

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3 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

4 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Based on laboratory animal studies, the manufacturing concentrate, 1-Methylcyclopropene MUP-HAIP, is of low acute toxicity, mildly irritating to the eyes, non-irritating to the skin, and is not a dermal sensitizer. Consequently, the signal words "CAUTION – EYE IRRITANT" are required on the label for the manufacturing concentrate.

Laboratory animal studies show that the end-use product, Harvista 1.3 SC, is of low acute toxicity, mildly irritating to the skin, minimally irritating to the eyes, and is not a dermal sensitizer. Consequently, the signal words "CAUTION – SKIN IRRITANT" are required on the label for the end use product.

Available information suggests that 1-Methylcyclopropene is rapidly absorbed and metabolized, and is unlikely to cause mutagenicity, genotoxicity, or prenatal developmental toxicity.

Furthermore, consideration was given to the anticipated low exposure potential resulting from the intended use of the product, as well as the dietary and occupational exposure aspects outlined below.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Based on the low toxicity of 1-Methylcyclopropene, as well as the volatility and environmental fate of the active ingredient, the dietary risk from food and drinking water is not a concern.

Risks in Residential and Other Non-Occupational Environments

Estimated risk for residential and other non-occupational exposure is not of concern.

Residential and non-occupational exposure of individuals coming in contact with Harvista 1.3 SC during application is not expected to result in unacceptable risk when Harvista 1.3 SC is used according to label directions.

Occupational Risks From Handling Harvista 1.3 SC

Occupational risks are not of concern when Harvista 1.3 SC is used according to the label directions, which include protective measures.

Occupational exposure to individuals handling Harvista 1.3 SC is not expected to result in unacceptable risk when the product is used according to label directions. Precautionary and hygiene statements on the product label aimed at mitigating worker exposure are considered adequate to protect individuals from any unnecessary risk due to occupational exposure.

Postapplication activities, such as scouting treated areas, may result in the exposure of workers re-entering areas treated with Harvista 1.3 SC. However, exposure is expected to be low when re-entry is restricted for 4 hours after application.

Bystander exposure is not expected to result in health risks of concern when the product is used according to label directions.

Environmental Considerations

What Happens When 1-Methylcyclopropene Is Introduced into the Environment?

1-Methylcyclopropene is not expected to pose risks of concern to the environment when used according to label instructions.

1-Methylcyclopropene will enter the environment when it is sprayed on apple trees to delay ripening before the apples are harvested. 1-Methylcyclopropene mixes readily in water and is expected to enter the atmosphere from moist soil and water surfaces. 1-Methylcyclopropene is expected to break down quickly in air through chemical reactions. 1-Methylcyclopropene is not expected to move through soil to groundwater. 1-Methylcyclopropene is not expected to persist or build-up in the environment and will not accumulate in the tissues of organisms.

1-Methylcyclopropene did not cause harmful effects to birds, small mammals, bees, earthworms, terrestrial plants and aquatic organisms. When used according to label directions, 1-methylcyclopropene is not expected to pose risks of concern to non-target terrestrial and aquatic organisms. No risk mitigation measures are required.

What Is the Value of Harvista 1.3 SC?

Harvista 1.3 SC is a plant growth regulator that slows fruit maturation, delays harvest and extends the marketing life of apples.

A single preharvest application of Harvista 1.3 SC to apples slows the loss of fruit firmness by inhibiting the ripening hormone, ethylene. The slower rate of fruit maturation can be expected to result in fruit quality that is maintained for a longer period of time. In turn, this can be expected to allow growers to optimally manage harvest and maximize the quantity of fruit harvested with better storage and marketing characteristics as compared to untreated fruit.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of Harvista 1.3 SC to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

The personal protective equipment for all loading, and/or application, as well as clean-up and repair activities required on the end-use product label includes a long-sleeved shirt, long pants, shoes, socks, chemical-resistant gloves, and goggles or a face shield. Care must be taken to avoid bystander exposure from drift during application, and entry into treated areas is restricted for 4 hours after applying Harvista 1.3 SC.

Environment

The labels for 1-Methylcyclopropene and related end-use product were updated to reflect current labelling standards. 1-Methylcyclopropene and its end-use product are not expected to pose risks of concern to the environment when used according to the label directions.

Next Steps

Before making a final registration decision on 1-Methylcyclopropene, the PMRA will consider any comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please note that, to comply with Canada's international trade obligations, consultation on the proposed MRLs will also be conducted internationally via a notification to the World Trade Organization. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

Other Information

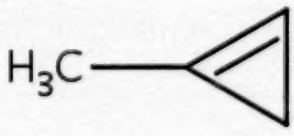
When the PMRA makes its registration decision, it will publish a Registration Decision on 1-Methylcyclopropene (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

1-Methylcyclopropene

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	1-Methylcyclopropene
Function	Plant growth regulator
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	1-Methylcyclopropene
2. Chemical Abstracts Service (CAS)	Cyclopropene, 1-methyl-
CAS number	3100-04-7
Molecular formula	C_4H_6
Molecular weight	54.09
Structural formula	
Purity of the active ingredient	97.2%

1.2 Physical and Chemical Properties of the Active Ingredient and End-Use Product

Technical Product—1-Methylcyclopropene Technical

Property	Result
Colour and physical state	Colourless gas
Odour	Sharp, light sweetish smell
Melting range	N/A
Boiling point or range	N/A
Density	2.24 g/L at 20°C
Vapour pressure at 20°C	2×10^5 Pa at 25°C
Ultraviolet (UV)-visible spectrum	No absorbance maxima observed above 205 nm.

Property	Result
Solubility in water at 20°C	137 mg/L at 20°C
Solubility in organic solvents at 20°C	Solvent — Solubility (g/L) acetone — 2.4 dichloromethane — 2.0 ethyl acetate — 12.5 heptane — 2.5 methanol — 11.25 xylene — 2.3
n-Octanol-water partition coefficient (K_{ow})	log K_{ow} = 2.4 (no pH effect)
Dissociation constant (pK_a)	The product contains no acid or base functionality.
Stability (temperature, metal)	Chemically unstable and begins to self-react immediately.

End-Use Product—1-Methylcyclopropene MUP HAIP

Property	Result
Colour	White and opaque
Odour	Odourless
Physical state	Powder
Formulation type	WP (wettable powder)
Guarantee	4.5%
Container material and description	HDPE or fiber drum with polyethylene coating/liner, 5-100 kg
Density	0.455-0.467 g/mL
pH of 1% dispersion in water	5.37
Oxidizing or reducing action	The product does not contain any oxidizing or reducing agents.
Storage stability	The product is stable for 14 days at 54°C or one year at 25°C stored in HDPE bottles.
Corrosion characteristics	No corrosion to HDPE bottles was observed when the product was stored at 54°C for 14 days or at 25°C for one year.
Explodability	The product was determined not to have explosive properties.

End-Use Product— Harvista 1.3 SC

Property	Result
Colour	Milky white
Odour	Garlic-like odour
Physical state	Liquid dispersion
Formulation type	Suspension concentrate (SU)
Guarantee	1.3%
Container material and description	HDPE or HDPE lined jugs, pails or totes, 2-2000 L
Specific gravity at 20°C	1.319
pH of 1% dispersion in water	5.65

Property	Result
Oxidizing or reducing action	The product is not expected to be an oxidizing or a reducing agent.
Storage stability	The product is stable for one year when stored in the HDPE container at 25°C.
Corrosion characteristics	No corrosion to the HDPE container was observed after one year storage at 25°C.
Explodability	The product does not contain any explosive components.

1.3 Directions for Use

Harvista 1.3 SC, containing 1.3% 1-Methylcyclopropene, is a plant growth regulator that is foliarly applied to apple trees from 3 to 21 days prior to the anticipated harvest date. Harvista 1.3 SC is applied at 5.9-17.7 L/ha (100-300 g a.i./ha) with 0.05% v/v (0.5 L/1000 L) Xiameter OFX-0309 Fluid Silicone Surfactant in a water volume of 50-600 L/ha using ground application spray equipment fitted with a direct chemical injection system. The water volume used is dependent on tree architecture, row spacing and canopy.

1.4 Mode of Action

The active ingredient, 1-Methylcyclopropene, competes with ethylene at membrane-bound ethylene receptor proteins within the fruit, thereby inhibiting both the action of ethylene and the synthesis of additional ethylene via a positive feedback mechanism from the ethylene-receptor complex. The inhibition of ethylene action and synthesis delays the onset of the climacteric period of fruit ripening in which ethylene production and respiration increase rapidly. The maturation of the fruit is, therefore, delayed with the result that fruit retains its firmness for a longer period.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

The methods provided for the analysis of the active ingredient and impurities in the technical product have been validated and assessed to be acceptable for the determinations.

2.2 Method for Formulation Analysis

The method provided for the analysis of the active ingredient in the formulation has been validated and assessed to be acceptable for use as an enforcement analytical method.

2.3 Methods for Residue Analysis

Refer to Regulatory Note REG2004-07, *1-Methylcyclopropene*, for a detailed assessment of analytical methods.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

Refer to the Regulatory Note REG2004-07, *1-Methylcyclopropene*, for a detailed assessment of the toxicology database for 1-Methylcyclopropene.

Absorption of ^{14}C-1-methylcyclopropene administered by gavage to rats was rapid and the elimination from the blood and plasma is considered to be biphasic. Although limited, distributed residues in the test animals were predominantly found in the liver and kidney of both males and females. 1-Methylcyclopropene and its metabolites do not bioaccumulate in the tissues sampled. The absorbed radioactivity was rapidly excreted. The majority of the 1-Methylcyclopropene administered was catabolized and exhaled as carbon dioxide, followed by elimination of the metabolites via the urine and then the feces.

Based on animal studies, the manufacturing concentrate, 1-Methylcyclopropene MUP-HAIP, was shown to have low toxicity via the oral, dermal and inhalation routes of exposure. 1-Methylcyclopropene MUP-HAIP was also determined to be mildly irritating to the eyes, non-irritating to the skin, and was not a dermal sensitizer.

In a short-term toxicity study, 1-Methylcyclopropene MUP-HAIP was administered to male and female rats in the diet for 90 days. A reduction in the body weight gain in the males for week 0 to 4 was observed in the high-dose group, as well as a decrease in food efficiency in the high-dose group of both males and females. Observed effects, including an increase in the relative liver weight in males, an increase in the amount of yellow-brown pigment (hemosiderosis) in macrophages in the red pulp of the spleen and an increase in reticulocyte count in both males and females, as well as an increase in hemoglobin distribution width, red blood cell count, hemoglobin, and hematocrit in female rats were not considered to be adverse. The LOAEL is 20,000 ppm (1290/1513 mg/kg bw/day in males/females), based on lower body weight gains. The NOAEL is 7500 ppm was set at 477/564 mg/kg bw/day in males/females.

Studies previously submitted to the PMRA examining the potential for prenatal developmental toxicity and genotoxicity of 1-methylcyclopropene were assessed. Refer to Regulatory Note REG2004-07, *1-Methylcyclopropene*, for the detailed assessment. Based on these findings, 1-Methylcyclopropene MUP-HAIP is not expected to be genotoxic or considered to be a prenatal developmentally toxic substance. The QSAR model, DEREK, did not pick up any alerts for 1-methylcyclopropene.

Based on animal studies, the end use product, Harvista 1.3 SC, is of low acute toxicity by the oral, dermal, and inhalation routes, is mildly irritating to the skin, minimally irritating to the eyes, and is not a dermal sensitizer.

The formulants in Harvista 1.3 SC are supported for the proposed uses.

Incident Reports

As of August 2016, no human or domestic animal incident reports involving 1-Methylcyclopropene had been submitted to the PMRA.

3.2 Occupational, Residential and Bystander Risk Assessment

3.2.1 Dermal Absorption

Dermal absorption of Harvista 1.3 SC is not expected to be of concern due to the low toxicity of the end use product via the dermal route.

3.2.2 Use Description

Harvista 1.3 SC is proposed for outdoor apple orchard use for the delay in maturity of apples by preventing perception of ethylene, a phytohormone responsible for fruit ripening and senescence. Harvista 1.3 SC is applied with ground application equipment from an injector nurse tank, preferably using flat-fan nozzles with a pressure that will result in moderately sized spray droplets (50 to 300 µm). Harvista 1.3 SC is to be applied 3 to 21 days before harvest and may be reapplied as long as the total does not exceed 300 g a.i./ha/season.

The amount of Harvista 1.3 SC applied by ground application equipment is 100 to 300 g a.i./ha. The quantity of a.i. handled by one individual per day is 2.0 to 6.0 kg a.i./day and a maximum total amount of 6.0 kg a.i./season, assuming the use of an airblast sprayer on 20 ha.

3.2.3 Mixer, Loader, and Applicator Exposure and Risk

Exposure to workers loading and applying Harvista 1.3 SC is expected to be short-term in duration and to occur primarily by the dermal route but inhalation and incidental ocular exposure to the eyes is also possible.

The risk due to exposure of Harvista 1.3 SC, and to any impurities in the end use product, from loading, applying, clean-up, and maintenance of machinery for workers is considered to be acceptable when used according to the label, which includes adhering to the label precautions.

3.2.4 Postapplication Exposure and Risk

There is a potential for exposure to workers re-entering areas treated with Harvista 1.3 SC. Given the nature of the postapplication activities typically performed (for example, scouting treated areas), dermal contact with treated apple trees is possible. While the degree of exposure will be related to the time of re-entry and the duration of the activities, the potential risk due to exposure resulting from postapplication work is not a concern, when re-entry is restricted for 4 hours after application.

3.2.5 Residential and Bystander Exposure and Risk

The use of Harvista 1.3 SC outdoors may result in bystander exposure due to drift. The risk due to bystander exposure will be mitigated by the inclusion of a buffer statement on the label, advising against application to areas of human habitation and activity unless consideration has been given to the wind speed, wind direction, temperature inversions, application equipment, and sprayer settings.

3.3 Food Residue Exposure Assessment

3.3.1 Food

Based on the low toxicity profile and toxicokinetics of 1-Methylcyclopropene, as well as the environmental fate of the active ingredient, no risk due to dietary exposure to residues of 1-methylcyclopropene is anticipated.

There is reasonable certainty that no harmful effects will result from dietary exposure to residues of 1-Methylcyclopropene, and associated impurities, from the proposed use in apple orchards, in the general population and potentially sensitive subpopulations, including infants and children.

3.3.2 Drinking Water

Although the end-use product will not be applied near or directly to water, some drinking water exposure may be possible through run-off from treated areas. Based on the vapour pressure (2.5×10^5 Pa) and Henry's law constant (4.37×10^9 Pa) for 1-Methylcyclopropene, volatilization from water is a more important route of dissipation than hydrolysis. The concentration of 1-Methylcyclopropene in the aquatic environment is expected to be negligible as it is a volatile gas product and preferentially partitions from the water into the atmosphere. In addition, toxicity to 1-methylcyclopropene is low. Consequently, the risk due to exposure from drinking water is not a concern.

3.3.3 Acute and Chronic Dietary Risks for Sensitive Subpopulations

Calculations of acute reference doses (ARfDs) and acceptable daily intakes (ADIs) are not required for 1-Methylcyclopropene. Based on all the available information and hazard data, the PMRA concludes that 1-Methylcyclopropene is of low toxicity. Thus there are no threshold effects of concern. As a result, there is no need to require definitive (multiple dose) testing or apply uncertainty factors to account for intra- and interspecies variability, safety factors or margins of exposure. Further factoring of consumption patterns among infants and children, special susceptibility in these subpopulations to the effects of 1-Methylcyclopropene, including neurological effects from pre- or postnatal exposures, and cumulative effects on infants and children of ammonium salt of fatty acid and other registered products containing 1-Methylcyclopropene, does not apply to this active ingredient. As a result, the PMRA has not used a margin of exposure (safety) approach to assess the risks of 1Methylcyclopropene to human health.

3.3.4 Aggregate Exposure and Risk

Based on the relevant information in the Agency's database, there is reasonable certainty that no harm will result from aggregate exposure of residues of 1-Methylcyclopropene to the general population in Canada, including infants and children, when Harvista 1.3 SC is used according to the label. This includes all anticipated dietary (food and drinking water) exposures and all other non-occupational exposures (dermal and inhalation) for which there is reliable information.

3.3.5 Maximum Residue Limits (MRLs)

As part of the assessment process prior to the registration of a pesticide, Health Canada must determine that the consumption of the maximum amount of residues that are expected to remain on food products when a pesticide is used according to label directions will not be a concern to human health. This maximum amount of residues expected is then legally specified as an MRL under the *Pest Control Products Act* for the purposes of adulteration provision of the *Food and Drugs Act*. Health Canada specifies science-based MRLs to ensure the food Canadians eat is safe.

The dietary risks from food and drinking water are not a concern given that Harvista 1.3 SC is of low acute toxicity. However, an MRL of 0.01 ppm for 1-Methylcyclopropene on apples was previously established and applies to the proposed new use on this crop.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

1-Methylcyclopropene will enter the environment when used as a preharvest foliar spray on apples to delay ripening. 1-Methylcyclopropene is a gas at ambient temperatures. For use in spray application to apples, it is manufactured in a powder form as a 1-methylcyclopropen. After mixing with water in the spray tank, it is expected to volatilise quickly once it enters the environment.

1-Methylcyclopropene is non-persistant in water-sediment systems when tested in a laboratory. 1-Methylcyclopropene has high solubility in water, has a high vapour pressure and, based on Henry's law constant, will readily volatilize from moist soil or water surfaces. Volatilisation is expected to be a major route of dissipation, however, 1-Methylcyclopropene is not expected to be persistent in the environment. Using computer modelling, it is estimated that 1-Methylcyclopropene would undergo rapid photo-oxidation in the atmosphere through reactions with ozone and hydroxyl radicals, with a half-life of 0.123 days following 12 hours of exposure to sunlight.

1-Methylcyclopropene was estimated to be mobile in soil based on modelling estimates, but soil leaching studies showed that the majority of the compound remained in the upper layers of the soil column. 1-Methylcyclopropene is not expected to bioaccumulate in biota based on a log K_{ow} of 2.4.

Environmental fate parameters are summarized in Appendix I, Table 4.

4.2 Environmental Risk Characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated environmental exposure concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (in other words, protection at the community, population, or individual level).

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC). If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Risks to Terrestrial Organisms

A summary of terrestrial toxicity data is presented in Appendix I, Table 5. The accompanying risk assessment is presented in Appendix I, Tables 7-8.

Bees (pollinators): Exposure to bees is typically assessed for contact with spray droplets during application or to residues found on the surface of leaves, as well as through the ingestion of pollen and nectar contaminated from direct spray (oral exposure). In laboratory tests, 1-methylcyclopropene showed no toxic effects on adult bees, *Apis mellifera,* on an acute oral and contact basis at the highest doses that were tested. The LOC (= 0.4) was not exceeded for toxicity via contact exposure. Based on dietary exposure estimates for bees, the LOC (= 0.4) was exceeded as the risk quotient was <5.8. However, as the highest dose tested did not cause effects, the results likely overestimate the RQ.

Based on the proposed use pattern for Harvista 1.3 SC and its propensity to volatilise readily, exposure of bees to 1-Methylcyclopropene is expected to be negligible. Therefore, 1-methylcyclopropoene is not expected to pose a risk to bees based on the following: 1-methylcyclopropene is applied to apples 3-21 days prior to harvest when bees are not actively foraging in the orchard canopy (no flowers); exposure to drift in adjacent areas where bees may be foraging on flowering plants will be less than the full application rate, and 1-methylcyclopropene is likely to volatilize quickly and be broken down in air by photochemical reactions.

Beneficial arthropods: 1-Methylcyclopropene caused no statistically significant adverse acute effects on species of parasitic wasp and predatory mite. The screening level risk quotients for both the parasitic wasp (*Aphidius rhopalosiphi*) and predatory mite (*Typhlodromus pyri*) were below the LOC (= 2).

Birds and mammals: At the highest dose tested, oral exposure to 1-methylcyclopropene caused no mortality or adverse effects in the northern bobwhite (*Colinus virginianus*) on an acute oral and reproductive basis. 1-Methylcyclopropene was shown to be practically non-toxic to rats on an acute oral basis. The RQs did not exceed the LOC for birds and mammals.

Non-target terrestrial plants: The toxicity of a formulation of 1-methylcyclopropene (AFxRD-038, 3.6-3.8% a.i. or AF-701, 1.3-1.4% a.i.) to non-target plants was determined through studies of vegetative vigour seedling emergence using ten standard crop species. No significant adverse effects were observed in any plant species at the highest application rate tested (300 g a.i./ha). Seedling emergence was not considered to be a relevant endpoint as application of 1-methylcyclopropene is in the fall (approximately August to October) when plants have matured and seedlings are not present in large quantities. The risk quotient calculated at the screening level did not exceed the LOC for vegetative vigour.

4.2.2 Risks to Aquatic Organisms

A summary of aquatic toxicity data is presented in Appendix I, Table 6. The accompanying risk assessment is presented in Appendix I, Table 9.

Freshwater invertebrates: 1-Methylcyclopropene showed no adverse effects to daphnids, *Daphnia magna*, on an acute basis at the concentrations that were tested. The risk quotient calculated at the screening level did not exceed the LOC on an acute basis.

Freshwater fish: 1-Methylcyclopropene showed no adverse effects to rainbow trout (*Oncorhynchus mykiss*) on an acute basis. The risk quotient calculated at the screening level did not exceed the LOC on an acute basis.

Amphibians: To assess the risk to amphibians, fish toxicity endpoints are used as surrogate data, when amphibian data are not available, to represent aquatic life-stages of amphibians. The difference between fish and amphibian risk assessments is related to the water depth used for the estimated environmental concentrations (water depth of 15 cm for amphibians). The screening level risk quotient for acute exposure of amphibian to 1-MCP did not exceed the LOC.

Freshwater algae and vascular plants: 1-Methylcyclopropene showed no adverse effects to the green alga, *Pseudokirchneriella subcapitata*, and vascular plant, duckweed, *Lemna gibba*. The risk quotients calculated at the screening level did not exceed the LOC.

4.2.3 Incident Reports

As of 18 November 2015, the PMRA has not received any incident reports that involved the active ingredient 1-Methylcyclopropene. There have been no new scientific studies received through the PMRA's incident reporting program for the active ingredient 1-Methylcyclopropene or any end-use products containing 1-Methylcyclopropene. As of 20 August 2014, the United States Environmental Protection Agency had not received any environmental incidents involving 1-Methylcyclopropene (EIIS database for American environmental incidents).

5.0 Value

5.1 Consideration of Benefits

The apple harvest can present growers with a number of challenges, including fruit that matures too quickly prior to adequate size and skin colour development, the need for multiple harvests of a single apple variety due to variable fruit maturation, and preharvest fruit drop. The degree to which one or more of these phenomena occurs varies by the growing season and/or apple variety, and result in lower returns to the grower as well as fruit of reduced quality for consumers.

As the fruit of any particular apple variety do not all mature at the same time, multiple harvests are usually required to ensure that fruit is picked at the desired level of maturity, whether for the immediate fresh market or for either short or long term storage. Application of Harvista 1.3 SC prior to the anticipated date of the first harvest can be expected to delay maturity of earlier fruit more than later fruit, thereby narrowing the harvesting window, particularly of varieties that are known to mature fruit over a long period of time. Minimizing variability results in a greater percentage of fruit being harvested in one pass and at the desired level of maturity thereby lowering costs to the grower while increasing the proportion of fruit in the higher quality grades.

Some apple varieties are prone to fruit drop, such as the commonly grown 'McIntosh'. Fruit that falls prior to harvesting (in other words, grounders), are typically used for juice and command a much lower price than tree-harvested fruit. Harvista 1.3 SC-treated trees can be expected to retain more fruit allowing time for additional colour and size development prior to harvesting at the desired level of maturity. This would be expected to maximize returns to the grower while providing the consumer with a more desirable product at the retail level.

Harvista 1.3 SC has been identified as an intermediate priority in the Canadian Grower Priority Database. As the use pattern for Harvista 1.3 SC is the same as that registered for apple in the U.S. (as AF-701), the availability of Harvista 1.3 SC will allow Canadian apple growers to more effectively compete with U.S. producers for both domestic and international markets by producing higher quality fruit with better storage characteristics and potentially reducing harvesting costs.

Aviglycine hydrochloride (AVG), also an ethylene inhibiting plant growth regulator, is the only preharvest alternative to 1-Methylcyclopropene to achieve some of the same effects in apples. AVG is applied four weeks prior to anticipated harvest to reduce fruit drop while potentially delaying fruit maturity and maintaining fruit quality, such as firmness. Harvista 1.3 SC has a wide application window and is primarily intended to slow fruit maturation and delay harvest, while potentially reducing fruit drop. Harvista 1.3 SC could be applied as an alternative to, or in conjunction with, AVG to maximize fruit retention, maturity and harvest delay, fruit quality and storability.

The application of Harvista 1.3 SC would not be expected to impact the selection of pest control products or strategies that may be used in integrated pest management systems in orchards to manage diseases and/or insect pests. A preharvest application of Harvista 1.3 SC could be followed by one or more postharvest, in storage, applications of a 1-Methylcycloproprene product to further slow ripening and of a fungicide to control postharvest diseases.

5.2 Effectiveness in Achieving the Desired Effects

The performance of Harvista 1.3 SC in slowing fruit maturity was evaluated in multiple trials conducted in apple orchards in Ontario as well as in both Washington and New York states. The trials were designed to evaluate the effect of one or more of application rate, timing, apple variety, spray volume and addition of surfactant on the efficacy of Harvista 1.3 SC in slowing fruit maturation. Indicators of advancing fruit maturity include fruit firmness loss, increased starch hydrolysis (greater conversion of starch to sugars resulting in a reduced starch pattern index), increased internal ethylene concentration and incidence of watercore, a physiological disorder usually associated with advancing maturity.

The effect of Harvista 1.3 SC in slowing fruit maturation was demonstrated as a slowing of fruit firmness loss and starch hydrolysis, a slowing in the rise of internal ethylene concentration, and as a delay in the onset and incidence of watercore. Higher rates within the rate range of 100 to 300 g a.i./ha were often observed to result in a greater response. Application of Harvista 1.3 SC between 3 and 21 days prior to harvest was demonstrated to be effective with a greater response sometimes observed when application was made closer to harvest. The addition of an organosilicone surfactant similar to Xiameter OFX-0309 Fluid Silicone Surfactant, at 0.05% v/v to the spray solution sometimes resulted in additional maturity delay, usually observed as increased firmness retention. While the degree of response to Harvista 1.3 SC was demonstrated to not be dependent on spray volume (in other words, dilution), the quantity of solution used to achieve good spray coverage will necessarily depend on such factors as row spacing, tree shape, height, and canopy volume. Several commonly grown varieties were collectively tested in these trials, including one in which the response of two varieties to an application of Harvista 1.3 SC was evaluated. In this trial, a delay in fruit maturity was observed for both varieties, but was manifested as a slowing of firmness loss for one, a slowing of starch hydrolysis for the other and a reduction in watercore incidence for both, indicating that response to Harvista 1.3 SC depends in part on apple variety, as reflected on the product label.

The results of these trials indicate that harvest can generally be delayed by 7 to 14 days since the level of fruit firmness, internal ethylene concentration and/or starch pattern index of Harvista 1.3 SC-treated apples harvested on a particular date was generally similar to that of untreated apples

harvested 7 to 14 days previously. As increasing levels of ethylene are known to promote fruit drop and slow fruit filling and skin colour development, application of Harvista 1.3 SC can be expected to result in greater fruit retention, larger fruit and improved skin colour. The ethylene inhibiting effect of Harvista 1.3 SC can also be expected to improve the storage potential of apples harvested from treated orchards.

Adequate information was submitted to support the efficacy claims that are summarized in Table 5.2.1.

Table 5.2.1 Performance Claims for Harvista 1.3 SC

Crop	Application Timing	Application Rate	Performance Claims
Apples	3-21 Days Before Anticipated Harvest	5.9-17.7 L/ha (100 – 300 g a.i./ha)[a] with the option to add 0.05% v/v (0.5 L/1000 L) Xiameter OFX-0309 Fluid Silicone Surfactant in a water volume of 50-600 L/ha	- reduction in fruit ethylene production - maintenance of fruit firmness - delayed starch hydrolysis - delayed onset and incidence of watercore - delay in fruit maturation - delay in harvest by 7-14 days - improved harvest management - reduction of preharvest fruit drop - enhanced storage potential - additional time for fruit colour and size development

a) within this range, lower rates should be used when fruit is at an earlier stage of maturity or for bicoloured apple varieties; higher rates are intended for use when fruit is at a more advanced stage of maturity except for bicoloured varieties.

5.3 Phytotoxicity to Host Plants

There were no signs of phytotoxicity in any of the efficacy trials. Apple trees can be expected to exhibit an adequate margin of tolerance to Harvista 1.3 SC when applied in accordance with the label instructions.

5.4 Supported Uses

The submitted value information was adequate to support all label claims for Harvista 1.3 SC applied to apples 3 to 21 days prior to harvest at 5.9 to 17.7 L/ha (100 to 300 g a.i./ha) with the option to include Xiameter OFX-0309 Fluid Silicone Surfactant at 0.05% v/v.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances [those that meet all four criteria outlined in the policy: that is, persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

During the review process, 1-Methylcyclopropene was assessed in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- 1-Methylcyclopropene does not meet all Track 1 criteria and it is not expected to form any transformation products that are Track 1 substances. 1-Methylcyclopropene is not expected to persist or bioaccumulate in the environment.

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*.[6] The list is used as described in the PMRA Notice of Intent NOI2005-01[7] and is based on existing policies and regulations including DIR99-03 and DIR2006-02,[8] and takes into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

- Technical grade 1-Methylcyclopropene, the manufacturing concentrate, 1-Methylcyclopropene, MUP-HAIP, and the end-use product Harvista 1.3 SC do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*.

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5 DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*

6 Canada Gazette, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613, Part 1 *Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions* and Part 3 *Contaminants of Health or Environmental Concern.*

7 NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act.*

8 DIR2006-02, *Formulants Policy and Implementation Guidance Document.*

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02.

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for 1-Methylcyclopropene is adequate to define the toxic effects that may result from exposure to 1-Methylcyclopropene. The technical grade active ingredient, 1-Methylcyclopropene (1-MCP) Technical, the manufacturing concentrate, 1-Methylcyclopropene MUP-HAIP, and the end-use product, Harvista 1.3 SC, are of low acute toxicity. 1-Methylcyclopropene MUP-HAIP is mildly irritating to the eyes and is non-irritating to the skin. Harvista 1.3 SC is minimally irritating to the eyes and mildly irritating to the skin. 1-Methylcyclopropene (1-MCP) Technical, 1-Methylcyclopropene MUP-HAIP, and Harvista 1.3 SC are not dermal sensitizers.

Loaders, applicators, and workers are not expected to be exposed to levels of 1-methylcyclopropene, and associated impurities, that will result in an unacceptable risk due to exposure when Harvista 1.3 SC is used according to label directions.

Bystander exposure is mitigated by observing the standard buffer statement on the label, advising against application to areas of human habitation and activity unless consideration has been given to the wind speed, wind direction, temperature inversions, application equipment, and sprayer settings.

The dietary risks from food and drinking water are not a concern given the low toxicity of Harvista 1.3 SC, the physical and chemical properties, and the environmental fate of 1-methylcyclopropene. An MRL of 0.01 ppm for use on apples has been established.

7.2 Environmental Risk

1-Methylcyclopropene is not expected to persist in the environment. 1-Methylcyclopropene, when used according to the label directions of the proposed end-use products, is not expected to pose risks of concern to the environment.

7.3 Value

The submitted value information is adequate to support all label claims for Harvista 1.3 SC when applied to apples 3 to 21 days prior to harvest at rates of 5.9 to 17.7 L/ha (100 to 300 g a.i./ha).

A single preharvest application of Harvista 1.3 SC to apples slows the rate of fruit maturation. The resulting delay in harvest can be expected to allow growers to optimally manage harvest and maximize the quantity of fruit harvested with better storage and marketing characteristics as compared to untreated fruit.

8.0 Proposed Regulatory Decision

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of 1-Methylcyclopropene (1-MCP) Technical and Harvista 1.3 SC to apple trees/orchards to slow ripening and delay harvest.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

List of Abbreviations

µg	micrograms
1/n	exponent for the Freundlich isotherm
a.i.	active ingredient
ADI	acceptable daily intake
ALS	acetolactate synthase
ARfD	acute reference dose
atm	atmosphere
bw	body weight
CAS	Chemical Abstracts Service
cm	centimetres
d	day
DF	dry flowable
DNA	deoxyribonucleic acid
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in concentration)
DT_{90}	dissipation time 90% (the dose required to observe a 90% decline in concentration)
EC_{25}	effective concentration on 25% of the population
EC_{50}	effective concentration on 50% of the population
ER_{25}	effective rate for 25% of the population
g	gram
ha	hectare(s)
HDT	highest dose tested
Hg	mercury
HPLC	high performance liquid chromatography
hrs	hours
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_d	soil-water partition coefficient
K_F	Freundlich adsorption coefficient
km	kilometre
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
L	litre
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LLNA	local lymph node assay
LOAEL	lowest observed adverse effect level
LOEC	low observed effect concentration
LOQ	limit of quantitation
LR_{50}	lethal rate 50%
mg	milligram
mL	millilitre
MAS	maximum average score

MIS	maximum irritation score
MOE	margin of exposure
MRL	maximum residue limit
MS	mass spectrometry
N/A	not applicable
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NOER	no observed effect rate
N/R	not required
NZW	New Zealand white
OC	organic carbon content
OM	organic matter content
Pa	Pascal
PBI	plantback interval
PHI	preharvest interval
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
REI	restricted-entry interval
RSD	relative standard deviation
SC	soluble concentrate
$t_{1/2}$	half-life
T3	tri-iodothyronine
T4	thyroxine
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
UAN	urea ammonium nitrate
UF	uncertainty factor
USEPA	United States Environmental Protection Agency
UV	ultraviolet
v/v	volume per volume dilution

Appendix I Tables and Figures

Table 1 Toxicity Profile of Harvista 1.3 SC Containing 1-Methylcyclopropene

(Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons)

Study Type/Animal/PMRA #	Study Results
Acute oral toxicity Rat, Fischer 344 PMRA # 2561755	LD_{50} ♀ > 5000 mg/kg bw Low toxicity
Acute dermal toxicity Rat, Fischer 344 PMRA # 2561756	LD_{50} ♂♀ > 5000 mg/kg bw Low toxicity
Acute inhalation toxicity Rat, Wistar PMRA # 2561757	LC_{50} ♂♀ > 5.31 mg/L Low toxicity
Eye irritation Rabbit, New Zealand White (♂) PMRA # 2561758	MAS [a] = 1.33/110 MIS [b] = 14.3/110 (1 hrs) MAS was not 0/110 by 24 hours. MIS was 0/110 by 72 hours. Minimally irritating
Skin Irritation Rabbit, New Zealand White (♀) PMRA # 2561759	MAS [a] = 2.0/8 MIS [b] = 3.0/8 (1 and 24 hrs) Mildly irritating
Dermal sensitization (LLNA) Mouse, CBA/J (♀) PMRA # 2561760	Negative Not a dermal sensitizer

[a] MAS = Maximum Average Score for 24, 48, and 72 hrs
[b] MIS = Maximum Irritation Score (average)

Table 2 Toxicity Profile of 1-Methylcyclopropene (1-MCP) Technical

(Effects are known or assumed to occur in both sexes unless otherwise noted)

Study Type/Animal/PMRA #	Study Results
Toxicokinetics (inhalation) Rat, Sprague Dawley PMRA # 565049	Absorption was rapid but limited. Twenty-four hours after administration the highest residues were predominantly found in the lung, liver, kidney spleen and fat respectively in both males and females. The absorbed radioactivity was rapidly excreted. The route and rate of excretion were independent of the sex or dose level. The majority of the test substance was inhaled and exhaled without being metabolized. The recovered radiolabelled compounds were too little to identify and/or quantify the metabolites.
Acute oral toxicity Acute dermal toxicity Eye irritation Dermal irritation Dermal sensitization PMRA # 565028, 565029, 565031, 565032, 565033	Based on the physical nature of 1-methylcyclopropene (gas at room temperature) waivers were requested and were granted.
Acute inhalation toxicity Rat, Crl:CD BR PMRA # 565030	LC_{50} ♂♀ > 2.5 mg/L Low toxicity
Short-term oral toxicity Short-term dermal toxicity PMRA # 565034, 565020	Based on the physical nature of 1-methylcyclopropene (gas at room temperature) waivers were requested and were granted.
Short-term inhalation toxicity (90 days) Rat, Crl:CD BR PMRA # 5650.38, 744381, 744382	NOAEL 9 mg/kg bw/day LOAEL 45 mg/kg bw/d An increase in absolute and relative liver weight in both sexes and an increase in kidney weight in females at the higher dose.

Study Type/Animal/PMRA #	Study Results
Prenatal developmental toxicity Rat, Crl:CD BR PMRA # 565043	Maternal NOAEL 45 mg/kg bw/d LOAEL 142 mg/kg bw/d Fetal NOAEL 440 mg/kg bw/d Maternal findings included darkened and enlarged spleens at the mid dose and a decrease in body weight during the first few days of treatment at the high dose. There were no adverse fetal findings.
Gene mutations in bacteria PMRA # 565045	Negative
Gene mutations in mammalian cells (*in vitro*) PMRA # 565046	Negative
Chromosome aberrations (*in vitro*) PMRA # 565047	Negative
Micronucleus assay (*in vivo*) PMRA # 565048	Negative

[a] MAS = Maximum Average Score for 24, 48, and 72 hrs
[b] MIS = Maximum Irritation Score (average)

Table 3 Toxicity Profile of 1-Methylcyclopropene MUP-HAIP

(Effects are known or assumed to occur in both sexes unless otherwise noted)

Study Type/Animal/PMRA #	Study Results
Toxicokinetics (oral) Rat, Sprague Dawley PMRA # 2561820	Absorption of ^{14}C-1-methylcyclopropene was rapid and the elimination from the blood and plasma was biphasic. Distributed residues in the test animal were predominantly found in the liver and kidney of both males and females. 1-methylcyclopropene and its metabolites do not bioaccumulate in the tissues sampled. The absorbed radioactivity was rapidly excreted. The majority of the ^{14}C-radiolabel was catabolized and exhaled as carbon dioxide, followed by elimination of the metabolites via the urine and then the feces.
Acute oral toxicity Rat, Wistar PMRA # 2561822	LD_{50} ♀ > 5000 mg/kg bw Low toxicity
Acute dermal toxicity Rat, Wistar PMRA # 2561824	LD_{50} ♂♀ > 5000 mg/kg bw Low toxicity

Study Type/Animal/PMRA #	Study Results
Acute inhalation toxicity Rat, Fischer 344 PMRA # 2561828	LC_{50} ♂♀ > 5.12 mg/L Low toxicity
Eye irritation Rabbit, New Zealand White (♂) PMRA # 2561829	MAS [a] = 3.89/110 MIS [b] = 11.7/110 (1 hrs) All scores were not 0/110 by 72 hours post-instillation. Mildly irritating
Skin Irritation Rabbit, New Zealand White (♀) PMRA # 2561830	MAS [a] = 0/8 MIS [b] = 0/8 Non-irritating
Dermal sensitization (LLNA) Mouse, CBA/J (♀) PMRA # 2561831	Negative Not a dermal sensitizer
90-Day short-term oral toxicity (diet) Rat, Crl:CD(SD) PMRA # 2561813	NOAEL = 7500 ppm (♂/♀: 477/564 mg/kg bw/day) LOAEL = 20,000 ppm (♂/♀: 1290/1513 mg/kg bw/day) Effects at 20,000 ppm included a decrease in overall body weight gain (weeks 0 to 4), an increase in the relative liver weight in males, and an increase in hemosiderosis in macrophages in the red pulp of the spleen.
Gene mutations in bacteria PMRA # 565045, 2561815	Refer to Table 2, Appendix 1.
Gene mutations in mammalian cells (*in vitro*) PMRA # 565046, 2561817	Refer to Table 2, Appendix 1.
Chromosome aberrations (*in vitro*) PMRA # 565047, 2561818	Refer to Table 2, Appendix 1.

Study Type/Animal/PMRA #	Study Results
Micronucleus assay (*in vivo*) PMRA # 565048, 2561816	Refer to Table 2, Appendix 1.
QSAR modelling (DEREK) PMRA # 2561832	No alerts identified.

[a] MAS = Maximum Average Score for 24, 48, and 72 hrs
[b] MIS = Maximum Irritation Score (average)

Table 4 Fate and Behaviour in the Environment

Property	Test substance	Value	Transformation products	Comments	PMRA#
Abiotic transformation					
Hydrolysis	1-MCP	NA	None	Self-reacted / volatilization at 50°C	565061
Laser photolysis (OH reaction)	1-MCP	4.4 hours	Not reported	Hydroxyl radical reactions in air may be an important route of transformation	565071
Photo-oxidation (Atkinson model[1])	1-MCP	0.123 days (12 hours exposure to OH radicals in sunlight)	Ozone Formaldehyde	Important route of tranformation in air	565063
Biotransformation					
Biotransformation in aerobic water sediment system	1-MCP	Bradford Creek water/sediment: $t_{½}$ < 6 hours; Lake Galena Inlet water/sediment: $t_{½}$ < 2 days	Methallyl alcohol and CO_2	Non persistent.	2561665
Mobility					
Adsorption / desorption in soil	1-MCP	HPLC estimated K_{oc}: 26.3	None	Very high soil mobility	2561662
Soil leaching	1-MCP	4 soils Layer 1: >82% AR* Layer 2: 1-5% AR Other layers: <3% AR	7 unknown minor transformation products	87% to 103% AR[2] of bound residues (non-extractable); 1-MCP is not expected to leach	2561666

[1] Calculated using the computer program OPWIN according to the model calculation of Atkinson.
[2] AR: Applied radiocativity

Table 5 Toxicity to Terrestrial Non-Target Species

Organism	Exposure	Test Substance	Endpoint value	Toxicity Classification	Reference PMRA#
Invertebrates					
Earthworm *Eisenia fetida*	Acute (in air), 14-d	1-MCP-αCD[A] (3.4% a.i.)	LD_{50} > 10 ppm (v/v) in air	NA	2561670
Honey bee *Apis mellifera*	Acute (in air), 48-h	1-MCP-αCD (3.3% a.i.)	LD_{50} > 10 ppm (v/v) in air NOEC = 10 ppm (v/v) in air	NA	2561671
	Acute contact, 48-h	AF-701[B] (1.3% a.i.)	LD_{50} > 150 µg product (>2.0 µg a.i./bee) NOEC = 2.0 µg a.i./bee	No adverse effects at the highest dose tested	2561767
	Acute oral, 48-h		LD_{50} > 115 µg product (>1.5 µg a.i./bee) NOEC = 1.5 µg a.i./bee	No adverse effect at the highest dose tested	2561768
Parasitic wasp *Aphidius rhopalosiphi*	Acute, 48-h	1-MCP-αCD (3.3% a.i.)	LR_{50} > 10 ppm (v/v) in air	NA	2561673
		AFxRD-038[C] (3.6% a.i.)	LR_{50} > 300 g a.i./ha	NA	2561674
Predatory mite *Typhlodromus pyri*	Acute, 7-d	1-MCP-αCD (3.3% a.i.)	LR_{50} > 10 ppm (v/v) in air	NA	2561672
Ground beetle *Poecillus cupreus*	Acute, 14-d	AFxRD-038 (3.8% a.i.)	LR_{50} > 300 g a.i./ha	NA	2561675
Birds					
Northern bobwhite *Colinus virginianus*	Acute oral, 14-d	AFxRD-038 (3.6% a.i.)	LD_{50} > 2250 mg product (>81 mg a.i./kg bw) NOEL = 81 mg a.i./kg	Practically non-toxic; No adverse effect at the highest dose tested	2561661
		AF-701 (1.3% a.i.)	LD_{50} > 13,192 mg product (>171 mg a.i./kg bw) NOEL = 171 mg a.i./kg bw		2561771
	Acute dietary, 8-d	AFxRD-038 (3.6% a.i.)	LC_{50} > 5620 mg product (>202.3 mg a.i. /kg diet) NOEC = 5620 mg product / kg diet		2561682

Organism	Exposure	Test Substance	Endpoint value	Toxicity Classification	Reference PMRA#
		AF-701 (1.3% a.i.)	LC_{50} > 11,000 mg product (>110 mg a.i./kg, measured) NOEC = 110 mg a.i./kg		2561772
	Reproduction, 21-wk	1-MCP-αCD (4.7% a.i.)	NOEL = 90.4 mg a.i./kg/day		2561681 / 2561840
Mallard duck *Anas platyrhynchos*	Acute dietary, 8-d	AFxRD-038 (3.6% a.i.)	LC_{50} > 5620 mg product (>202.3 mg a.i. /kg diet) NOEC = 5620 mg product / kg diet		2561683
Mammals					
Rat	Acute oral, 14-d	1-MCP-αCD (3.4% a.i.)	LD_{50}>5000 mg product (>170 mg a.i./kg bw)	No adverse effect at highest dose tested	565050
Vascular plants					
Multiple species (10)[D]	Seedling emergence, 21-d	AF-701 (1.4% a.i.)	ER_{25} >300 g a.i./ha ER_{50} > 300 g a.i./ha NOER = 300 g a.i./ha LOER > 300 g a.i./ha	NA	2561773
		AFxRD-038 (3.6% a.i.)	ER_{25} = 256 g a.i./ha ER_{50} > 300 g a.i./ha NOER = 75 g a.i./ha (dw tomato, most sensitive)	NA	2561686
	Vegetative vigor, 21-d	AF-701 (1.39% a.i.)	ER_{25} > 300 g a.i./ha ER_{50} > 300 g a.i./ha NOER = 300 g a.i./ha LOER > 300 g a.i./ha	NA	2561774
		AFxRD-038 (3.6% a.i.)	ER_{25} > 300 g a.i./ha ER_{50} > 300 g a.i./ha NOER = 300 g a.i./ha	NA	2561688

[A] 1-MCP-αCD: 1-Methylcyclopropene alpha cyclodextrin complex

[B] AFxRD-038: Formulation of 1-methylcyclopropene (3.6-3.8% a.i.)

[C] AF-701: Formulation of 1-methylcyclopropene (1.3-1.4% a.i.).[D] Onion (*Allium cepa*), ryegrass (*Lolium perenne*), wheat (*Triticum aestivum*), corn (*Zea mays*), cabbage (*Brassica oleracea*), cucumber (*Cucumis sativa*), soybean (*Glycine max*), lettuce (*Lactuca sativa*), tomato (*Lycopersicon esculentum*), radish (*Raphanus sativus*).

Table 6 Toxicity to Aquatic Non-Target Species

Organism	Exposure	Test Substance	Endpoint value (mg a.i./L)	Toxicity Classification	References PMRA#
Daphnia magna	Acute, 48 h	1-MCP-αCD[A] (3.3% a.i.)	EC_{50} > 0.776 NOEC = 0.776	No adverse effect at the highest concentration tested	2561677
		AFxRD-038[B] (3.6% a.i.)	EC_{50} > 0.678 NOEC = 0.678		2561676
		AF-701[C] (1.3% a.i.)	EC_{50} > 4.3 (measured) NOEC = 4.3		2561769
Rainbow trout *Onchorhynchus mykiss*	Acute, 96 h	1-MCP-αCD (3.3% a.i.)	LC_{50} > 0.966 NOEC = 0.966	No adverse effect at the highest concentration tested	2561678
		AFxRD-038 (3.6% a.i.)	LC_{50} > 0.750 NOEC = 0.750		2561679
		AF-701 (1.3% a.i.)	LC_{50} > 4.5 (measured) NOEC = 4.5		2561770
Green algae *Pseudokirchneriella subcapitata*	Acute, 96 h	1-MCP-αCD (3.3% a.i.)	EC_{50} > 0.838 NOAEC = 0.838	NA	2561685
		AFxRD-038 (3.6% a.i.)	EC_{50} > 0.576 NOAEC = 0.576	NA	2561684
Duckweed *Lemna gibba* G3	Acute, 7 d	MUP-HAIP[D] (4.24% a.i.)	EC_{50} >11 (measured) NOEC = 3.0 (frond yield, frond # growth rate)	NA	2561690 / 2561841

[A] 1-MCP-αCD: 1-Methylcyclopropene alpha cyclodextrin complex;
[B] AFxRD-038: Formulation of 1-methylcyclopropene (3.6-3.8% a.i.)
[C] AF-701: Formulation of 1-methylcyclopropene (1.3-1.4% a.i.);
[D] MUP-HAIP: manufacturing use product HAIP containing 4.24% of 1-methylcyclopropene

Table 7 Screening level and refined risk to bees, beneficial arthropods and terrestrial vascular plants

Organism	Exposure	Endpoint value	EEC	RQ[a]	LOC[b] exceeded
Invertebrates					
Bee	Oral	>1.5 µg a.i./bee	8.7 µg a.i./bee[c]	<5.8	Yes
	Contact	>2.0 µg a.i./bee	0.72 µg a.i./bee[d]	<0.36	No
Parasitic wasp[e] *(Aphidius rhopalosiphi)*	Contact	48-h LR_{50}> 300 g a.i./ha	300 g a.i./ha	<1	No
Vascular plants					
Multiple species	Vegetative vigour	ER_{25} > 300 g a.i./ha	300 g a.i./ha	<1	No

[a] An uncertainty factor of 1 is applied to bees, other terrestrial arthropods and terrestrial vascular plants.
[b] Level of Concern (LOC): 0.4, bees; 2, predatory and parasitic beneficial insects; 1, terrestrial plants.
[c] An EEC for oral toxicity to bees is calculated by multiplying the single application rate, in units of kg (i.e., 0.3 kg a.i./ha) by a factor of 29 µg a.i./bee, which gives an EEC in units that match the toxicity endpoint (µg a.i./bee)
[d] An EEC for contact toxicity to bees is calculated by multiplying the single application rate, in units of kg (i.e., 0.3 kg a.i./ha) by a factor of 2.4 µg a.i./bee, which gives an EEC in units that match the toxicity endpoint (µg a.i./bee).
[e] Most sensitive species of studies that were submitted.

Table 8 Screening level risk assessment to birds and mammals

Organism	Toxicity Value (mg a.i./kg bw/d)[A]	Feeding Guild (food item)	EDE[B] (mg a.i./kg bw)	RQ	LOC[C] exceeded
Small Bird (0.02 kg)					
Acute	81.00	Insectivore	24.42	0.30	No
Reproduction	90.40	Insectivore	24.42	0.27	No
Medium Sized Bird (0.1 kg)					
Acute	81.00	Insectivore	19.06	0.24	No
Reproduction	90.40	Insectivore	19.06	0.21	No
Large Sized Bird (1 kg)					
Acute	81.00	Herbivore (short grass)	12.31	0.15	No
Reproduction	90.40	Herbivore (short grass)	12.31	0.14	No
Small Mammal (0.015 kg)					
Acute	170.00	Insectivore	14.04	0.08	No
Medium Sized Mammal (0.035 kg)					
Acute	170.00	Herbivore (short grass)	27.24	0.16	No
Large Sized Mammal (1 kg)					
Acute	170.00	Herbivore (short grass)	14.56	0.09	No

[A] LD_{50}/LC_{50} value was used for acute endpoints and no uncertainty factor was applied because no effects were seen at the highest test concentration; thus, it was considered to be equivalent to the NOEL/NOEC value where no uncertainty value is applied.
[B] EDE = Estimated dietary exposure; is calculated using the following formula: (FIR/bw) × EEC, where
FIR: Food Ingestion Rate. For generic birds with body weight less than or equal to 200 g, the "passerine" equation was used; for generic birds with body weight greater than 200 g, the "all birds" equation was used:
Passerine Equation (body weight ≤200 g): FIR (g dry weight/day) = $0.398(\text{bw in g})^{0.850}$
All birds Equation (body weight >200 g): FIR (g dry weight/day) = $0.648\ (\text{bw in g})^{0.651}$
For mammals, the "all mammals" equation was used: FIR (g dry weight/day) = $0.235(\text{bw in g})^{0.822}$

bw: Generic Body Weight
EEC: Concentration of pesticide on food item. At the screening level, relevant food items representing the most conservative EEC for each feeding guild are used.
[C] Level of Concern (LOC) is 1 for birds and mammals.

Table 9 Screening level risk to aquatic organisms

Organism	Exposure	Endpoint value (mg a.i./L)	EEC (mg a.i./L)	RQ	LOC[A] exceeded
Freshwater species					
Daphnia magna	Acute 48-h	EC_{50} / 2 >0.339[B]	0.0375	<0.1	No
Rainbow trout (*Onchorhynchus mykiss*)	Acute 96-h	LC_{50} = 0.75[C]	0.0375	0.05	No
Amphibian	Acute	LC_{50} = 0.75[C]	0.2	0.26	No
Freshwater alga, *Pseudokirchneriella subcapitata*	Acute 96-h	EC_{50}/2 >0.288[B]	0.0375	<0.13	No
Vascular plants, *Duckweed, Lemna gibba* G3	7-d, Dissolved in test medium	EC_{50} /2 >5.5[B]	0.0375	<0.007	No

[A] Level of Concern (LOC) is 1 for aquatic organisms.
[B] Uncertainty factor of 2 was applied to the toxicity value from the study (see Table 8) for calculating the risk quotient (RQ).
[C] LC_{50} value was used for acute endpoints and no uncertainty factor was applied because no effects were seen at the highest test concentration; thus, it was considered to be equivalent to the NOEL/NOEC value where no uncertainty value is applied.

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3.0 Environment

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4.0 Value

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B. Additional Information Considered

i) Published Information

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2.0 Human and Animal Health

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